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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/512,926	02/25/2000	Fred S. Lamb	P-1057	6913

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EXAMINER

KIM, JENNIFER M

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/512,926	Applicant(s) LAMB, FRED S.	
	Examiner Jennifer Kim	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,6-11,23 and 25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,6-11,23 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7/26/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed July 26, 2004 have been received and entered into the application.

Action Summary

The rejection of claim 25 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of Applicants' amendment.

The rejection of claims 1,6-11 and 23 under 35 U.S.C. 112, first paragraph is withdrawn in view of Applicants' amendment.

The rejection of claim 25 under 35 U.S.C. 102(b) as being anticipated by Stromberg (U.S. Patent No. 5,470,883) evidenced by Kifor et al. (U.S. Patent No. 5,658,936) is withdrawn in view of Applicants' amendment.

The rejection of claims 1, 6-11 and 23 of record under 35 U.S.C. 103(a) over Grainger et al. of record is withdrawn in view of Applicants' amendment.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action.

Claim Rejections - 35 USC § 103

Claims 1, 6-11 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grainger et al. (U.S. Patent No. 6,197,789 B1) of record.

Grainger et al. teach tamoxifen is useful to prevent or treat conditions characterized by **inappropriate or pathological activity of endothelial cells**. (column 6, lines 5-10). Grainger et al. teach tamoxifen **inhibits vascular smooth muscle cells contraction**. (column 17, lines 35-47). Grainger et al. teach tamoxifen is useful on vascular smooth muscle cells to inhibit the pathological activity of the smooth muscle cells, and to inhibit the activation of **endothelial cells associated with vascular surgery, diabetes, hypertension, and coronary artery blockage**. (abstract, column 4, lines 7-16, column 5, line 65 through column 6, line 30, column 7, lines 15-33, column 8, lines 11-20, column 10, lines 51-57, column 15, line 54, column 18, lines 34-44, column 24, lines 47-50, and column 25, lines 4-8). Grainger et al. teach the procedural vascular traumas including **surgical procedures** include vascular surgery (e.g. **angioplasty, coronary bypass**) and the pathologies (**atherosclerosis, myocardial infraction and stroke**) can be prevented by the administration of tamoxifen. (column 3, lines 30-51, column 4, line 8-25).

Grainger et al. do not expressly teach the normalization of contractile response set forth in claim 1.

It would have been obvious to one of ordinary skill in the art to modify the teaching of Grainger et al. and employ tamoxifen to normalize the contractile response of vasculature in Grainger et al. patients since the teaching of "inhibiting contraction"

encompasses the "normalization" since the effect of inhibiting contraction encompasses the "normalization" since the effect of inhibition of the contraction of vascular smooth muscle would "normalize" the contraction of the patients disclosed by Grainger et al.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grainger et al. (U.S. Patent No. 6,197,789 B1) as applied to claims 1, 6-11 and 23 above and further in view of Stormberg (U.S. Patent No. 5,470,883).

Grainger et al. as applied as before.

Grainger et al. do not teach norepinephrine causing the contractile response of vasculature set forth in claim 25.

Stormberg teaches a method of **inhibiting or reversing** the peripheral vasoconstrictive effect of **norepinephrine** set forth in Applicants claim 25 by the oral administration of tamoxifen citrate. (column 2, lines 1-5). Stormberg teaches a method of **blocking or reversing vasoconstriction**, including peripheral vasoconstrictive effects of an intentionally or an unintentionally administered adrenergic agent such as norepinephrine to a subject who receives an injection of such adrenergic agent in a peripheral vascular area is administered a pharmacologically acceptable dose of tamoxifen citrate to inhibit or reverse the peripheral vasoconstrictive effect of the adrenergic agent (i.e. norepinephrine). (column 2, lines 6-16).

It would have been obvious to one of ordinary skill in the art to employ tamoxifen to normalize the contractile response of vasculature comprising a vascular smooth muscle cell layer and a compromised endothelial cell layer caused by norepinephrine

because Stromberg teaches tamoxifen is useful for reversing (normalizing) the vasoconstrictive effect of norepinephrine and because Grainger et al. teach that tamoxifen is useful for inappropriate or pathological activity of vascular smooth muscle cells and endothelial cells. One would have been motivated to employ tamoxifen to reverse (normalize) the contractile response of norepinephrine to achieve inhibition of contraction of vasculature caused by norepinephrine and to treat inappropriate or pathological activity of vascular smooth muscle cells or endothelial cells as taught by Grainger et al.

Response to Arguments

Applicant's arguments filed July 26, 2004 have been fully considered but they are not persuasive. Applicant argues a person of ordinary skill in the art reading the Grainger et al. patent would not have been motivated to normalize vasoconstriction of vasculature having a compromised endothelial layer by administering tamoxifen since Grainger et al. patent fails to provide any evidence that tamoxifen can affect vasoconstriction and a person of ordinary skill in the art would appreciate that contractile and proliferative VSMC serve different purposes, see, Owens(1995) and Lamb and Barna teaches the uncertainty of tamoxifen would affect VSM associated with vasculature having a compromised endothelial layer. This is not persuasive because the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references

themselves or in the knowledge generally available to one of ordinary skill in the art. In this case, Grainger et al. clearly teaches treatment of conditions characterized by inappropriate or pathological activity of **vascular smooth muscle cells** or **endothelial cells** by inhibition of contraction. (column 6, lines 5-10, column 17, lines 35-50). It is noted that instant claims are drawn to same "vascular smooth muscle cell" as taught by the cited art. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims allowed.

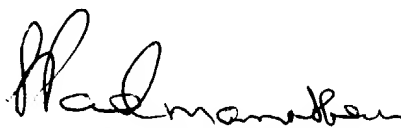
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

Jmk
November 23, 2004